REMARKS

Claims 1-23 are currently pending in the application. Claims 8-19 have been withdrawn by the Examiner as drawn to a nonelected invention. Claims 4 and 6 are newly amended to reduce their claim dependency. Claims 20-22 have been added to recite the subject matter removed from newly amended claims 4 and 6. No new matter has been added. Claims 1-7 and claim 20-23 are under consideration.

Claims rejection 35 U.S.C. 101

Claims 1-7 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial utility or a well established utility. Applicants respectfully traverse, and request reconsideration of the rejection in light of the comments below as applied to the instant claims and to newly added claims 20-23.

The specification discloses that the polypeptide of SEQ ID NO:2 is a UTP receptor, that incubation of cells expressing the polypeptide of SEQ ID NO:2 with UTP causes the accumulation of inositol tri-phosphate in Figure 4, and that an agonist or antagonist may be used in a pharmaceutical composition in the treatment of cystic fibrosis, also acknowledged by the office action. The Office Action further states that these utilities are not specific nor substantial because they do not identify or reasonably confirm a real world context of use.

Applicants respectfully contend that treating cystic fibrosis is a real world use. The office action further states that the disclosure does not establish a causative link between the polypeptide of SEQ ID NO:2 and cystic fibrosis, and that further research would be necessary to establish a causative link between the polypeptide of SEQ ID NO:2 and cystic fibrosis.

The standard for utility as outlined in the following excerpt from Section 2107.03 of the MPEP:

> As a general matter, evidence of pharmacological or other biological activity of a compound will be relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility. *Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881 (CCPA 1980). An applicant can establish this reasonable correlation by relying on statistically relevant data documenting the activity of a compound or composition, arguments or reasoning, documentary evidence (e.g., articles in scientific journals), or any combination thereof. The applicant does not have to prove that a

> correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use. *Nelson v. Bowler*, 626 F.2d 853, 857, 206 USPQ 881, 884 (CCPA 1980).

Applicants assert herein that there is a reasonable correlation between the activity in question (UTP mediated signaling of $P2Y_4$ (SEQ ID NO:2)), and the asserted utility (treating cystic fibrosis.

UTP as a therapeutic for Cystic Fibrosis

It was well known prior to the filing date of the instant application, that UTP was considered as a therapeutic for Cystic Fibrosis, as evidenced by the University of Wisconsin's web site (Oct 6, 2006) attached as Appendix 1 ,

> "Since it is known that with CF the chloride channels do not function properly, researchers have been exploring ways to activate alternative chloride channels. In 1991, researchers administered the drug Uridine Triphosphate, or UTP, by nasal spray to people with CF and observed that the exchange of salts (sodium and chloride) and water in their nasal cells had improved." paragraphs 1 and 2.

Further, a 1991 article by Knowles et al. (NEJM 325:533-538) teaches that extracellular UTP nucleotides are effective in vivo chloride secretagogues in the nasal epithelia of patients with cystic fibrosis, see abstract, attached as Appendix 2.

P2Y4 (SEQ ID NO:2) and Cystic Fibrosis

Merten et al. (1998) (Eur. J. Biochem. 251:19-24) teaches that cystic fibrosis results from mutation in a gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR) that lead to a defect in cAMP stimulated chloride transport, see first paragraph on page 19, attached as Appendix 3. Saleh et al. (1999) (Infection and Immunity 67(10):5076-5082) teach that human tracheal gland serous cells express CFTR and are able to respond to nucleotides through nucleotide receptor $P2Y_4$ with an increase in chloride transport, see first full paragraph on page 5077, attached as Appendix 4. Robaye et al. (2003) (Molec. Pharm. 63(4):777-783) teach that the UTP and ATP induced chloride secretory responses observed in

wild-type mice are abolished in $P2Y_4$-null mice, see abstract, in their work to evaluate the pharmocotherapeutic potential of the $P2Y_4$ receptor in the treatment of cystic fibrosis, attached as Appendix 5.

Robaye et al. teaches prior to the effective filing date of the instant application, it was known that one important action of extracellular ATP and UTP is to stimulate the transepithelial secretion of chloride as a result of increased apical permeability, referencing a 1991 article by Knowles, see first paragraph of discussion. Robaye et al. also teaches that this process is mediated by an inositol triphosphate mediated increase in cystolic Ca+2 that induces the opening of outwardly rectifying chloride channels, referencing a 1994 article by Clarke et al., see first paragraph of Robaye et al.'s discussion, consistent with the instantly disclosed accumulation of inositol tri-phosphate upon incubation of cells expressing the polypeptide of SEQ ID NO:2 with UTP (Figure 4 of the instant specification).

The combined teachings of these references provide a reasonable correlation between the activity in question (UTP signaling mediated through cell surface $P2Y_4$ (SEQ ID NO:2)), and the asserted utility (treating cystic fibrosis). That is, the actions of extracellular nucleotides (UTP) are mediated by $P2Y_4$ receptors as disclosed in the specification, and that $P2Y_4$ receptors are a pharmocotherapeutic target for the treatment for cystic fibrosis, as asserted in the specification. Therefore, Applicant submits there is disclosed a real world link between the claimed antibodies to $P2Y_4$ (SEQ ID NO:2), and the asserted utility of their being used as a pharmaceutical composition in the treatment of cystic fibrosis. In light of these remarks, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims rejection 35 U.S.C. 112, first paragraph, enablement

Claims 1-7 are rejected under 35 USC 112, first paragraph. The office action states that since the claimed invention is not supported by a specific and substantial asserted utility, nor a well established utility, ... one skilled in the art clearly would not know how to use the claimed invention.

Applicants respectfully traverse the rejection of claims 1-7, and as would be applied to newly added claims 20-23. Applicants contend the claimed invention is supported by a specific,

substantial and credible utility for the reasons described above, and therefore, contend an enablement rejection based on lack of utility should not be maintained.

Claims rejection - 35 U.S.C. 112, first paragraph, written description

Claims 2-7 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time of the application was filed, had possession of the claimed invention. Applicants respectfully traverse the rejections in view of the following remarks as applied to the instant claims, and as would apply to newly added claims 20-23.

The Office action states that the instant specification does not adequately support the scope of claims 2-5, drawn to an isolated antibody that specifically binds to a receptor comprising the amino acid sequence of SEQ ID NO:2, wherein said antibody is an agonist or antagonist of said receptor, nor claims 6 and 7, drawn to a pharmaceutical composition comprising the antibody, because the specification fails to provide a representative number of species of the claimed genus.

In *Enzo Biochem, Inc. v. GenProbe Inc.*, 296 F.3d 1316, 63USPQ2d 1609 (Fed. Cir. 2002), the court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics.... i.e., complete or partial structure, or other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics." (emphasis omitted, bracketed material in original). The holdings of this case is also applicable to the instant claims.

The structure of antibodies and monoclonal antibodies were well known at the time of the invention, including the partial structure, i.e. that of an antibody framework. The functional characteristics of the claimed antibodies, i.e. the antibodies' ability to binding to the protein of SEQ ID NO:2, and/or acting as an antagonist or agonist of the protein's function is disclosed. Because the structure and functional properties of the claimed antibodies are disclosed in the

instant specification, they meet the written description requirements as set forth in *Enzo Biochem, Inc. v. GenProbe Inc.*, supra.

Further, Example 16 of the Written Description Guidelines issued by the USPTO provides an example where the specification contemplates, but does not teach in an example, antibodies which specifically bind to a novel antigen X. The Guidelines conclude that: considering the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized that the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X. Because the instant disclosure meets the above criteria with respect to the antigen $P2Y_4$, Applicants submit that the disclosure meets the requirement under 35 USC 112, first paragraph, as providing an adequate written description of the claimed invention.

Further, the structure of agonist and antagonist antibodies were well established at the time of the invention. One of skill in the art would be able to select for agonist and antagonist antibodies of $P2Y_4$ by measuring the level of inositol tri-phosphate the incubation of cells expressing the polypeptide of SEQ ID NO:2 with UTP, see Figure 4 of the specification. Because the specification "describes the invention with sufficient relevant identifying characteristics that such a person skilled in the art would recognize that the inventor had possession of the claimed invention" (*Pfaff v. Wells Electronics*, Inc. 525 U.S. 55), Applicants respectfully submit that Applicants were in possession of the claimed antibody molecules, and respectfully request reconsideration of the rejection.

Conclusion

Applicants submit that in view of the foregoing remarks, all issues relevant to patentability raised in the Office Action have been addressed. Applicants respectfully request the withdrawal of rejections over the claims of the present invention.

Respectfully submitted,

Amy DeClerque 54849 (AmyDeClerq)

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Name: Kathleen Williams
Registration No.: 34,380
Customer No.: 29933
Edward Angell Palmer & Dodge LLP
P.O. Box 55874
Boston, MA 02205
Telephone No.: Tel. (617) 439-4444